REMARKS

Rejections

Claim 17 stands rejected under 35 U.S.C. 112, second paragraph, for use of the term "molecule".

Claims 1, 3-6, 9-14, 16-20, 29, and 30 stand rejected under 35 U.S.C. 102(b) as being anticipated by WO 97/49387.

Claims 1, 3-6, 9-11, 16-20, 29, and 30 stand rejected under 35 U.S.C. 102(b) as being anticipated by EP 552 802.

Claims 1, 2, 10, 12, 17, and 19 stand rejected under 35 U.S.C. 102(e) as being anticipated by U.S. 6,008,184 ("Pluyter").

Claims 1, 2, 10, 12, 17, and 19 stand rejected under 35 U.S.C. 102(a) as being anticipated by U.S. 5,891,468 ("Martin").

Claims 1, 3-6, 9-14, 16-20, and 27-30 stand rejected under 35 U.S.C. 103(a) as being obvious over WO 97/49387 by itself or in combination with Martin.

The Claimed Invention

The claimed invention includes vesicles made from triblock amphiphilic ABA copolymers, where one of A or B is hydrophilic and the other is hydrophobic, which self-assemble when dispersed in oil or water. The vesicles are hollow. Vesicles are defined on page 4 as "spontaneously forming aggregates having a generally spherical shape and an interior void." The resulting vesicles will have hydrophobic and hydrophilic layers arranged depending on the type of copolymer used.

The claimed invention further includes nanocapsules formed by stabilizing the vesicles made from ABA copolymers. The nanocapsules are also hollow. Stabilization can be through crosslinking of the copolymers, such as crosslinking of end groups of the copolymers.

The claimed invention further includes nanocapsules formed by end-group stabilization of amphiphilic copolymers. The copolymers do not have to be triblock copolymers.

Active agents can be encapsulated within the vesicles and the nanocapsules and targeting molecules can be attached to the vesicles and nanocapsules.

Analysis

112 Rejection

The Examiner maintains the rejection of claim 17, his argument being that it is indefinite due to use of the term "molecule". Claim 17 is directed to incorporation of a molecule into the vesicle membrane. It would be possible to incorporate one molecule, such as one membrane protein. The Examiner states that the issue is not with the term molecule but simply the use of the term in the singular. Applicants do not believe that they should amend claim 17 to state that multiple molecules are incorporated but have amended to state that "one or more molecules" may be incorporated.

102 Rejections

WO 97/49387

The Examiner did not find language in WO 97/49387 specifically stating that the nanoparticles are solid- that the interior core domain is not a void. The Examiner points to language on page 13, line 25 where it is said that micelles can have the shape of vesicles (note that the definition of "particles" also states that they can have the shape of vesicles. Neither definition states that the micelles or particles are hollow, or that they are vesicles- simply that they can have the shape of vesicles.

It is agreed that 97/49387 does not literally state that the nanoparticles are solid, however it is evident from statements in the specification and the related US patent that the nanoparticles are not hollow.

The inventors, Wooley et al., describe the prior art on page 3, lines 6-20 as "core-shell type polymer nanoparticles having a crosslinked core". They then go on to state that "Until now, attempts to prepare core-shell type polymer nanoparticles having a crosslinked shell domain and an interior core domain have been unsuccessful." The invention is just that- nanoparticles having a crosslinked shell domain and interior core domain- where the interior core domain may also be crosslinked. Amphiphilic copolymers are used to form the particles- wherein the hydrophilic portion forms the shell domain and the hydrophobic portion forms the interior core domain, or vice versa.

See also on page 15, lines 11-14 and 24-26, where it is stated that in some embodiments, the interior core domain can be crosslinked. See also on page 72, lines 7-

11: "The methods of preparing the particles of the present invention employ amphiphilic copolymers, the blocks of which in either the crosslinked shell domain or the interior core domain can be independently or together either homogeneous or heterogeneous." In other words, the interior core domain is contains blocks of the amphiphilic copolymer and the particles is not hollow. Moreover, throughout the application the inventors suggest crosslinking the interior core domain (see page 72, lines 19-22, for example).

Also see the claims of the issued related US patent, No. 6,383,500, for example claim 1 (emphasis added):

> 1. A particle comprising an amphiphilic copolymer and having a core and a crosslinked shell which differs from said core in hydrophilicity and hydrophobicity, said shell comprising a region of said copolymer which differs in hydrophilicity and hydrophobicity from **another region of said copolymer in said core**, said copolymer being crosslinked in said region within said shell, said copolymer region in said shell having a degree of crosslinking ranging from about 1% to about 80%, said copolymer being selected from among amphiphilic copolymers physically conducive to forming micelles prior to crosslinking.

Micelles are commonly formed from amphiphilic molecules, having a hydrophilic (or hydrophobic) head region and a hydrophobic (or hydrophilic) tail region. The amphiphilic molecules assemble into spherical structures wherein the heads are on the periphery of the micelle and the tails are clustered in the interior. The interior is not a void- micelles are not hollow.

Methods of making the nanoparticles are described beginning on page 69. One method involves assembling the amphiphilic copolymers into a micellar structure and then crosslinking the outer hydrophilic or hydrophobic heads. As discussed above, micelles are not hollow- the tail regions are clustered in the interior. These tail regions can be crosslinked together, in one embodiment.

The inventors on the present application can file a declaration, if that would help.

The Examiner also states that the present claims are limited to hollow particles. Applicants clearly define the term "vesicles" on page 4 of the application as "spontaneously forming aggregates having a generally spherical shape and an interior void." Nonetheless, the claims have been amended to specifically state that the vesicles are hollow.

Accordingly, the reference does not anticipate the claimed vesicles or nanocapsules and this rejection is traversed.

Claim 17

After the shells of the particles described in WO 97/49387 are crosslinked, the crosslinked shells of the particles are either hydrophilic or hydrophobic. They do not posses an amphiphilic nature per se that allows them to form a membrane-like superstructure similar to biological membranes as the amphiphilic polymers do in the vesicles and nanocapsules of the present invention. Accordingly, the structures described in WO 97/49387 do not allow a functional incorporation of natural membrane proteins. Such proteins would be of crucial importance to target the particles or to enable them to 'communicate' with their environment.

EP 552 802

EP 552 802 also describes polymerizable copolymer micelles. The copolymer has a water soluble component and an oleophilic component. As stated on page 4, line 6, the oleophilic component in the core is crosslinked, increasing the stability of the chemically fixed micelles. In other words, the core is not hollow but rather comprises crosslinked copolymer.

Pluyter

The present claims are to vesicles comprising membranes formed from amphiphilic copolymers and nanocapsules formed from the vesicles. The term comprising refers to the vesicles- the vesicles can contain membranes formed from amphiphilic copolymers as well as other substances. Pluyter does not teach membranes formed from amphiphilic copolymers. Rather, Pluyter teaches lamellar vesicles which may have copolymers "partially incorporated" therein (col. 5, lines 51-55). The copolymers may be attached to the vesicles or incorporated within the vesicles but they do not form the vesicle.

Martin

The Examiner makes the same argument for Martin as for Pluyter- that it anticipates the claimed vesicles since it teaches vesicles formed from some other material which have a copolymer included therein. The present claims specifically recite that the

vesicle is formed from ABA amphiphilic copolymers. A reference teaching vesicles simply having an amphiphilic copolymer bound thereto or incorporated therein does not anticipate the claims.

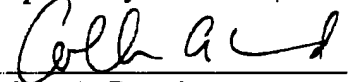
103 Rejection

Martin does not teach stabilizing vesicles to form nanocapsules. WO 97/49387 does not teach hollow vesicles. Accordingly, these references, taken alone or in combination, do not anticipate nor render the claimed invention obvious. This rejection is traversed.

Conclusion

None of the references that were cited teach or suggest hollow vesicles or nanocapsules formed from triblock amphiphilic copolymers. None of the references teach or suggest nanocapsules formed by end group crosslinking vesicles formed from amphiphilic copolymers. Accordingly, it is respectfully submitted that the references are not appropriate as the basis of rejection of the claims.

Respectfully submitted,



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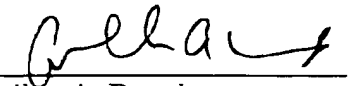

Collen A. Beard

Date: December 23, 2002

Claims as Amended

1. (Twice Amended) Hollow vesicles [Vesicles] comprising membranes formed from amphiphilic copolymers having hydrophobic and hydrophilic segments, wherein the copolymers are ABA copolymers, and wherein one of A and B is hydrophobic and the other is hydrophilic.

3. (Once Amended) Hollow nanocapsules [Nanocapsules] formed by stabilization of the vesicles of claim 1.

4. (Twice Amended) Hollow nanocapsules [Nanocapsules] formed by stabilization of vesicles comprising membranes formed from amphiphilic copolymers having hydrophobic and hydrophilic segments, wherein the vesicles are stabilized by end group polymerization of the copolymers.

5. The nanocapsules of claim 3, wherein the vesicles are stabilized via crosslinking of the copolymers.

6. The nanocapsules of claim 4, wherein the copolymers are AB copolymers, wherein one of A and B is hydrophobic and the other is hydrophilic.

9. The nanocapsules of claim 4, wherein an active agent is encapsulated within the nanocapsule.

10. The vesicles of claim 1, wherein an active agent is encapsulated within the vesicle.

11. The nanocapsules of claim 3, wherein an active agent is encapsulated within the nanocapsule.

12. The vesicles of claim 1, wherein the vesicles comprise a hydrophilic inner layer, a hydrophobic middle layer and a hydrophilic outer layer.

13. The vesicles of claim 1, wherein the vesicles comprise a hydrophobic inner layer, a hydrophilic middle layer and a hydrophobic outer layer.

14. The vesicles of claim 1, wherein the copolymers are U-shaped and the vesicles have a hydrophobic inner layer and a hydrophilic outer layer, or a hydrophilic inner layer and a hydrophobic outer layer.

16. The nanocapsules of claim 4, wherein the polymerization is via photopolymerization.

17. (Once Amended) The vesicles of claim 1, wherein one or more molecules are [a molecule is] incorporated into the vesicle membrane.

18. The nanocapsules of claim 3, wherein the hollow morphology of the nanocapsules is preserved when the nanocapsules are dry.

19. The vesicles of claim 1, wherein the vesicles are biodegradable.

20. The nanocapsules of claim 3, wherein the nanocapsules are biodegradable.

27. The vesicles of claim 1 further comprising targeting molecules bound to the surface of the vesicles.

28. The vesicles of claim 27 wherein the targeting molecules are selected from the group consisting of carbohydrates, proteins, folic acid, peptides, peptoids, and antibodies.

29. The nanocapsules of claim 4, wherein the hollow morphology of the nanocapsules is preserved when the nanocapsules are dry.

30. The nanocapsules of claim 4, wherein the nanocapsules are biodegradable.

Clean Copy of Claims as Amended

1. (Twice Amended) Hollow vesicles comprising membranes formed from amphiphilic copolymers having hydrophobic and hydrophilic segments, wherein the copolymers are ABA copolymers, and wherein one of A and B is hydrophobic and the other is hydrophilic.

3. (Once Amended) Hollow nanocapsules formed by stabilization of the vesicles of claim 1.

4. (Twice Amended) Hollow nanocapsules formed by stabilization of vesicles comprising membranes formed from amphiphilic copolymers having hydrophobic and hydrophilic segments, wherein the vesicles are stabilized by end group polymerization of the copolymers.

5. The nanocapsules of claim 3, wherein the vesicles are stabilized via crosslinking of the copolymers.

6. The nanocapsules of claim 4, wherein the copolymers are AB copolymers, wherein one of A and B is hydrophobic and the other is hydrophilic.

9. The nanocapsules of claim 4, wherein an active agent is encapsulated within the nanocapsule.

10. The vesicles of claim 1, wherein an active agent is encapsulated within the vesicle.

11. The nanocapsules of claim 3, wherein an active agent is encapsulated within the nanocapsule.

12. The vesicles of claim 1, wherein the vesicles comprise a hydrophilic inner layer, a hydrophobic middle layer and a hydrophilic outer layer.

13. The vesicles of claim 1, wherein the vesicles comprise a hydrophobic inner layer, a hydrophilic middle layer and a hydrophobic outer layer.

14. The vesicles of claim 1, wherein the copolymers are U-shaped and the vesicles have a hydrophobic inner layer and a hydrophilic outer layer, or a hydrophilic inner layer and a hydrophobic outer layer.

16. The nanocapsules of claim 4, wherein the polymerization is via photopolymerization.

17. (Once Amended) The vesicles of claim 1, wherein one or more molecules are incorporated into the vesicle membrane.

18. The nanocapsules of claim 3, wherein the hollow morphology of the nanocapsules is preserved when the nanocapsules are dry.

19. The vesicles of claim 1, wherein the vesicles are biodegradable.

20. The nanocapsules of claim 3, wherein the nanocapsules are biodegradable.

27. The vesicles of claim 1 further comprising targeting molecules bound to the surface of the vesicles.

28. The vesicles of claim 27 wherein the targeting molecules are selected from the group consisting of carbohydrates, proteins, folic acid, peptides, peptoids, and antibodies.

29. The nanocapsules of claim 4, wherein the hollow morphology of the nanocapsules is preserved when the nanocapsules are dry.

30. The nanocapsules of claim 4, wherein the nanocapsules are biodegradable.